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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/208,619	12/08/98	HILLMAN J	PF-0229-1DIV

EXAMINER

HM12/1215

HARRIS, A

ART UNIT	PAPER NUMBER
1642	12

LEGAL DEPARTMENT
INCYTE GENOMICS, INC.
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DATE MAILED: 12/15/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/208,619	Hillman And Goll
Examiner	**Group Art Unit**
Alana M. Harris, Ph. D.	1642

☒ Responsive to communication(s) filed on *October 2, 2000.*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *2-10 and 17-43* is/are pending in the applicat

Of the above, claim(s) *2-10, 19-31, and 34-43* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *17, 18, 32, and 33* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Response to Amendment

1. Claims 2-10 and 17-43 are pending.

Claims 2-10, 19-31 and 34-43, drawn to non-elected inventions are withdrawn from examination.

Claims 17, 32 and 33 have been amended.

Claims 17, 18, 32 and 33 are examined on the merits.

Specification

2. The disclosure is no longer objected to because the misspelled word, "protozoan"has been corrected.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Rejections

Claim Rejections - 35 U.S.C. § 112

4. The rejection of claims 17 and 18 under 35 U.S.C. 112, second paragraph, in Paper No. 9, mailed May 24, 2000 as being indefinite for failing to particularly point out and distinctly claim the

subject matter which applicant regards as the invention is withdrawn in view of Applicants' arguments.

Maintained Rejections

Claim Rejections - 35 U.S.C. § 112

5. The rejection of claims 32 and 33 under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement commensurate with the scope of the claimed invention is maintained. Please note that claims 17 and 18 of record in Paper 9, mailed May 24, 2000 are withdrawn due to Applicants' amendments to the recited claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The Applicants argue that "...more recent cases, ...have tended to accept a limitation such as 'an effective amount' as being definite when read in light of the supporting disclosure and in the absence of any prior art which would give rise to uncertainty about the scope of the claim." This is not found persuasive. Applicant is reminded that the claims define the subject matter of the invention and that the specification cannot be relied upon to read limitations into the claims. Arguments presented that rely on particular distinguishing features are not persuasive when the features or the endpoint of are not recited in the claims. As the claims read there is still uncertainty as to what function is to be achieved by an "effective amount". The rejection is maintained for the reasons stated and the rejection of record in Paper No. 9, mailed May 24, 2000.

6. The rejection of claims 17 and 18 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained. The reasons for maintaining the rejection are of record in Paper No. 9, mailed May 24, 2000 and set forth in the next paragraph.

Applicants argue that amendments to claim 17 further clarifies it and encompasses two well-defined categories of fragments deemed biologically active and immunologically active. And while Applicants suggest that with the definition of these fragments and assays that could be used in order to measure biological activity of the recited fragments the claims are still drawn to a large genus of molecules. While the specification discloses the structural features of the polypeptide sequence of SEQ ID NO:1 there is still no disclosure on the genus of polypeptides that the claim reads on and these subgenera still would have varying characteristics. Granted assays would provide information on whether or not the subgenera displayed a specific activity or function. However, Applicant has yet to assert information that reasonably conveys to one skilled in the art that the inventors had possession of the infinite number of polypeptide fragments that are claimed at the time the application was filed.

7. Claims 17, 18, 32 and 33 remain rejected under 35 U.S.C. 112, first paragraph specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons forthcoming, one skilled in the art clearly would not know how

to use the claimed invention. The reasons for this rejection are of record in paper no. 9, mailed May 24, 2000.

8. The rejection of claims 32 and 33 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained.

a. The phrase "effective amount" in claim 32 is vague and indefinite when the claims fail to state the function which is to be achieved. Applicants argument to the rejection have been discussed above. The question still remains what is the effective amount for?

Claim Rejections - 35 U.S.C. § 101

9. The rejection of claims 17 and 18 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility, a credible or a well established utility is maintained.

The Applicants argue that the "...bases for the rejection are improper," and the polypeptide, SEQ ID NO:1 termed HuTIM17 shares extensive amino acid identity with human preprotein translocase and with yeast mitochondrial inner membrane protein 17. Applicants also state that northern analysis shows the expression of HuTIM17 in libraries prepared from a wide variety of cell and tissues and the claimed invention has numerous practical, beneficial uses in toxicology testing, drug development, and the diagnosis of disease. This is not found persuasive. There is no objective evidence of record to show that HuTIM17 can be used in the treatment of

infections by protozoan parasites, as well as disorders caused by AIDS and cancer. Additionally mere expression in a tissue does not mean treatment.

Applicant argue that in view of the above arguments, the claimed invention has utility. Applicant has not correlated the claimed polypeptide, SEQ ID NO:1 to any such use. As stated in Brenner v. Manson (383 U.S. 519, 535-536, 148 USPQ 689, 693, 696 (1966)) "[i]t was never intended that a patent be granted upon a product..unless such product be useful" and "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion". Applicants in their specification are merely "hunting" and has not provided any successful conclusion.

Applicant argues that they have established a "well-established" utility. Since there is no correlation between the claimed products and a specific use, the Examiner disagrees.

Applicants argue that the genes are tools used in expression profiling (see page 13 of response). "Tools" are merely used to "hunt" with and do not provide any successful conclusion.

Applicants argue that the claimed invention is known to be useful because whole classes of genes are routinely incorporated for use in toxicology testing and expression profiling. Expression profiling is used to identify drug targets and characterize disease. While that is true what are the conditions caused by HuTIM17? If applicant cannot demonstrate any objective evidence to show that HuTIM17 causes any conditions, then one skilled in the art would not only have to see which drugs can change the activity of HuTIM17 but also would have to determine the condition. And clearly undue experimentation would be required to do this.

Applicants argue that just because the invention belongs to a broad class that does not negate its utility. The Examiner never said it did. In fact, the Examiner is looking at the specific protein and its relationship to other known proteins. While the PTO does issue patents to broad classes there is well-established, substantial and specific utility for those broad classes.

Additionally, the Applicants argue that the claimed invention's uses as a tool for toxicology testing is a practical and real-world use, hence it is a "substantial" use. There is no objective evidence of record to show that this claimed novel protein can be used to treat infections caused by protozoa or cancer. Furthermore, the sequence analysis shown on page 12, lines 12 and 13 asserts that HuTIM17 shares 75% amino acid sequence identity with human preprotein translocase and 48% amino sequence identity with yeast mitochondrial inner membrane protein 17 with no known apparent uses. Furthermore, characterizations based on structural/functional relationships have many problems. Bork (Genome Research 10:398-400, 2000) clearly teaches the pitfalls associated with comparative sequence analysis for predicting protein function because of the known error margins for high-throughput computational methods. Bork specifically teaches that computational sequence analysis is far from perfect, despite the fact that sequencing itself is highly automated and accurate (p. 398, col 1). One of the reasons for the inaccuracy is that the quality of data in public sequence databases is still insufficient. This is particularly true for data on protein function. Protein function is context dependent, and both molecular and cellular aspects have to be considered (p. 398, col 2). Conclusions from the comparison analysis are often stretched with regard to protein products (p. 398, col 3). Furthermore, recent studies show that alternative splicing might affect more than 30% of human

genes and the number of known post-translational modifications of gene products is increasing constantly so that complexity at protein level is enormous. Each of these modifications may change the function of respective gene products drastically (p. 399, col 1). Further, although gene annotation via sequence database searches is already a routine job, even here the error rate is considerable (p. 399, col 2). Most features predicted with an accuracy of greater than 70% are of structural nature and at best only indirectly imply a certain functionality (see legend for table 1, page 399). As more sequences are added and as errors accumulate and propagate it becomes more difficult to infer correct function from the many possibilities revealed by database search (p. 399 para bridging cols 2 and 3). The reference finally cautions that although the current methods seem to capture important features and explain general trends, 30% of those feature are missing or predicted wrongly. This has to be kept in mind when processing the results further (p. 400, para bridging cols 1 and 2).

Applicant argues that requiring applicant to state a particular utility misstates the law. The Examiner never required applicant to state such--applicant stated the utility in the specification and the Examiner is asking for objective evidence to support this.

Leef

Claim Rejections - 35 U.S.C. § 102

10. The rejection of claim 17 under 35 U.S.C. 102(b) as being anticipated by Accession Numbers P39515, Q02310, Maarse et al. (FEBS Letters 349:215-221, 1994, Reference #5 on IDS) and Ryan et al. (Mol. Biol. Cell 5:529-538, 1994, Reference #4 on IDS) is maintained.

Applicants argue that "...claim 17 as amended herein recites a biologically-active fragment

has HuMIM17 activity...", hence the 102 has been overcome. This is found unpersuasive. "HuMIM17" is a laboratory designation and while the abbreviation may have some notion of the activity of the protein, there is nothing in the claim which distinctly claims the protein. Applicant should particularly point out and distinctly claim the protein by claiming characteristics associated with the claimed invention. Hence, all of the recited references disclose a purified polypeptide comprising an amino acid sequence that is a biologically-active fragment of the amino acid sequence of SEQ ID NO:1, wherein said biologically-active fragment has HuMIM17 activity.

11. The rejection of claim 17 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent #5,876,991 (filed Feb. 21, 1997) is maintained. Applicants arguments have been discussed above. U.S. Patent #5,876,991 (see columns 85 and 86, Table 9) continues to disclose a purified polypeptide comprising an amino acid sequence that is a biologically-active fragment of the amino acid sequence of SEQ ID NO:1, wherein said biologically-active fragment has HuMIM17 activity. The rejection is maintained for the reasons set forth above.

12. The rejection of claim 32 under 35 U.S.C. 103(a) as being unpatentable over Accession Numbers P39515, Q02310, Maarse et al. (FEBS Letters 349:215-221, 1994, Reference #5 on IDS) and Ryan et al. (Mol. Biol. Cell 5:529-538, 1994, Reference #4 on IDS) and U.S. Patent #5,876,991, in view of Harlow and Lane (Antibodies, A Laboratory Manual, Cold Spring Harbor Laboratory, 1988) is maintained. Applicants argue that the 102 references do not teach a biologically-active fragment of the amino acid sequence of SEQ ID NO:1, wherein said

biologically-active fragment has HuMIM17 activity. This is found unpersuasive. As previously discussed, the aforementioned references do teach the limitations of claim 17. Hence, the 103 rejection stands..

New Grounds of Rejection

13. Claims 17 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The recitation "HuMIM17" in claim 17 is vague and indefinite. Likewise, is the recitation "HuTIM17". These abbreviations are not well known in the art. The applicant is advised to amend the claims to include the full terminology.

14. Claims 18 and 33 are free of the art.

Conclusion

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this office action. Accordingly, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris whose telephone number is (703)306-5880. The examiner can normally be reached on Monday through Friday from 6:30 am to 3:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703)308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703)308-0196.

Alana M. Harris, Ph.D.
Patent Examiner, Group 1642
December 14, 2000

Sheela J. Huff
SHEELA HUFF
PRIMARY EXAMINER